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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/914,292 | 08/27/2001 | Naoki Shinozuka | 159-68 | 4014 |

7590 12/04/2002
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| EXAMINER | |
| GUO, LYNDIA T | |
| ART UNIT | PAPER NUMBER |

1651
DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/914,292

Applicant(s)

SHINOZUKA ET AL.

Examiner

Lynda T Guo

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Status of the Application

The IDS PTO-1449 (Paper No. 3) received on 11 July 2002 has been entered.

Claims 1-5 are pending in the present Application.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,468,416 B1 in view of Burd et al. USPN 5,639,672.

In the instant Application, Claims 1-5 are drawn to a method of quantifying a substrate in a sample with the use of a biosensor. The claimed method comprises a dehydrogenase, a coenzyme, an electron mediator, a tetrazolium salt and the sample whereby the product, formazan, is detected by the biosensor, which comprises a working electrode and a counter electrode.

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USPN 6,468,416 B1 discloses of a method for quantifying a specific substrate, L-phenylalanine, in a sample with the use of a biosensor identical to those disclosed in the present Application. (See Figure 1 and description of Application and Figure 1 and description of the patent.) The method disclosed in USPN 6,468,416 B1 comprises a dehydrogenase, a coenzyme, and an electron mediator. The sensor also comprises a working electrode and a counter electrode. (See Abstract; Column 3, lines 1-19 and Claims 1-3.) What USPN 6,468,416 B1 does not disclose is the use of tetrazolium salt or the measurement of formazan product to quantitate the substrate. However, USPN 5,639,672 does disclose of a method of electrochemically quantifying fructosamine by measuring the **formazan** formed after the reduction of a **tetrazolium salt**. (See Column 6, lines 7-9 and Claims 9-10.) USPN 5,639,672 teaches that using mediators (including tetrazolium salts) adds sensitivity to the assay (see Column 4, lines 19-20). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a tetrazolium salt into the reaction for added sensitivity. Additionally, USPN 6,468,416 B1 is a species of the present Application. Thus, the genus (i.e. the present Application) is obviated by the species.

Specification

3. The disclosure is objected to because of the following informalities: on page 6, lines 8-9, the phrase, "the tetrazolium salt reacting finally" is awkward and unclear.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are drawn to a method of quantifying a substrate. Said Claims only specify that an enzyme reaction and a redox reaction occur and then an electrode is used to detect the product, formazan. There is no statement of how the measurement of formazan correlates to the substrate of interest. The Claims are thus incomplete and indefinite. Standard method steps in any assay include contacting, determining and correlating.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Burd et al. USPN 5,639,672.

Claims 4 and 5 are drawn to a method of quantifying a substrate and a biosensor, comprising a working electrode and a counter electrode made of electrically conductive materials integrated with the reaction reagents. The product measured by the biosensor is formazan after a potential

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is applied to the said formazan. The substrate quantified is listed in Claim 2, and is drawn to a plethora of substances.

Burd et al. discloses of a biosensor used in a method for measuring fructosamine, which involves measuring the current passed at a fixed voltage (i.e. applied potential) and the said biosensor comprises an anode (the working electrode) and a cathode (the counter electrode) made of a conductive material (e.g. carbon paste, graphite, silver, gold and others). Additionally, the reagents are coated onto the biosensor, i.e. the reagents and the electrodes are in an integrated system. (See Column 6, lines 7-9; Column 7, lines 45-50, 64; Column 8, lines 25-39; Column 9, lines 49-53 and Claims 1-3.)

Because Burd's disclosure clearly encompasses all the limitations set for in Claims 4 and 5, the said Claims are consequently rejected.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burd et al. (USPN 5,639,672) in view of Ishiyama et al. (EP 0908453 A1).

NOTE: The publication date for EP 0908453 A1 is 14 April 1999. The publication date for JP 09286784 A is 04 November 1997. The two documents are believed to be equivalent, so for the purposes of this office action, the English version (EP 0908453 A1) is relied upon.

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Claims 1-3 are drawn to a method of quantifying a substrate in a sample comprising a dehydrogenase, a coenzyme, an electron mediator, a tetrazolium salt and the sample, whereby the product, formazan, is detected.

Burd discloses of a method of quantifying a **substrate**, fructosamine, in which the reaction utilizes an oxidoreductase enzyme (e.g. fructosamine **dehydrogenase**) along with a **coenzyme** (NAD+) (see Column 6, lines 56-59). Although in the above specific example, Burd does not disclose the use of a tetrazolium salt as one of the reagents, Burd does teach that when using oxidoreductase enzymes, mediators can optionally be used (Column 4, lines 23-24) and the disclosed mediators include electron mediators such as phenazine as well as tetrazolium salts (Column 6, line 1). Burd further discloses that when a tetrazolium salt is used in the reaction, the resultant formazan is measured at an electrode (see Column 6, lines 7-9). Burd does not explicitly disclose the use of two mediators together, as taught by Applicant's present Application (e.g. use of an electron acceptor such as 1-methoxyphenazine methosulfate **and** a tetrazolium salt). However, Burd does state that, "the mediators can be combined with the enzymes" (Column 7, line 30) which suggests the use of multiple mediators. In another disclosure, Ishiyama et al. teaches that, "Quantitative measurement of various dehydrogenases, such as lactate dehydrogenase...alcohol dehydrogenase, and glutamate dehydrogenase, have conventionally been conducted by using **tetrazolium salt** compounds." Ishiyama further teaches that, "A property of the tetrazolium salt compound is its ability to receive a hydrogen released by the action of a dehydrogenase...via an intermediate **electron transporter** such as reduced nicotinamide-adenine dinucleotide...to give a corresponding formazan compound." (See page 2, paragraph 2.) In other words, Ishiyama teaches that, the reaction that converts a tetrazolium salt

into a formazan necessitates the use of an electron mediator, i.e. the two are dependent on one another.

In summary, Applicant's claims are to a quantitation method via a reaction comprising a dehydrogenase, a coenzyme, an electron mediator and a tetrazolium salt. Burd teaches a method comprising a dehydrogenase, a coenzyme and optionally a tetrazolium salt. Ishiyama teaches that, reactions comprising a dehydrogenase and a tetrazolium salt require an additional electron mediator to form the formazan product. Thus, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to include an additional electron mediator when using a tetrazolium salt in the reaction as taught by Burd in order to utilize the formazan product as an indirect means to measure a dehydrogenase substrate.

In regards to Claim 2, which is drawn to a list of substrates, all the listed compounds are known substrates for dehydrogenases. Claim 2 is rejected because Ishiyama et al. (EP 0908453 A1) discloses of lactate dehydrogenase, alcohol dehydrogenase, and glutamate dehydrogenase (Page 2, lines 11-12). All the other substrates not disclosed by Ishiyama are obviated because, lacking evidence to the contrary, each of the listed substrates would work the same way with its corresponding dehydrogenase.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynda T Guo whose telephone number is (703) 605-1200. The examiner can normally be reached on Mon - Fri (8:00am - 4:30pm).

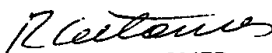
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on (703) 308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Lynda T Guo
Patent Examiner
November 27, 2002



RALPH GITOMER
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